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SCHNIZER, RICHARD A	

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/919,504
Filing Date: July 31, 2001
Appellant(s): EMANUELE ET AL.

EMANUELE ET AL.
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 12/30/05 appealing from the Office action mailed 12/1/04.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

This appeal involves claims 1-42.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is incorrect.

The amendment after final rejection filed on 2/4/2005 has been entered.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner. After further consideration, the rejections of claims 1, 2, 5, 8, 17-20, 23, 26, 41 under 35 USC 103 as obvious over Pahlson (1986) in view of Woodard (1989) is withdrawn. Also, the rejection of claims 3, 4, 9-13, 16, 21, 22, 27-31, 33, 35, 36, and 38 under 35 USC 103 as obvious over Pahlson (1986) and Woodard (1989) as applied to claims 1, 2, 5, 8, 17-20, 23, 26, 41, and further in view of Jansen (1990) is withdrawn. These rejections required an unduly broad interpretation of the claims.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,359,054	Lemieux	3-2002
5,674,911	Emanuele	10-1997
5,656,611	Kabanov	8-1997

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 8-13, 16-23, 26-31, 33-36, 38, and 41 are rejected under 35 U.S.C. 102(e) as being anticipated by Lemieux et al (US Patent 6,359,054, issued 3/19/02, filed 1/8/99).

Lemieux taught methods of delivering to an animal a composition comprising octablock block copolymers and nucleic acids, (see e.g. claim 13 at column 49). The nucleic acid can be an expression vector, antisense, ribozyme, or oligonucleotide (see column 21, lines 15-29). The octablock copolymers useful in the invention include a variety of conventional and reverse orientation octablock copolymers set forth at column 15, lines 8-29, including Pluronics T1101, T1301, T1501 and T110R1, T130R1, and T150R1. Pluronic T1501 corresponds to the octablock copolymer recited in instant claims 1, 2, and 17-20, and comprises a hydrophobe weight of 7000 Da and hydrophobe percentage of 90. Pluronic T1301 corresponds to the copolymer in instant

claims 3, 4, 21, and 22, and comprises a hydrophobe weight of 5500 Da and hydrophobe percentage of 90. Pluronic T1101 corresponds to the copolymer in instant claims 4 and 22, and comprises a hydrophobe weight of 4400 Da and hydrophobe percentage of 90. Pluronic T150R1 corresponds to the copolymer in instant claims 9, 10, 27, 28, 33, and 34, and comprises a hydrophobe weight of 6700 Da and hydrophobe percentage of 90. Pluronic T130R1 corresponds to the copolymer in instant claims 11, 12, 29, 30, 35, and 36, and comprises a hydrophobe weight of 5700 Da and hydrophobe percentage of 90. Pluronic T110R1 corresponds to the copolymer in instant claims 12, 30, and 36, and comprises a hydrophobe weight of 4800 Da and hydrophobe percentage of 90.

Thus Lemieux anticipates the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6, 7, 9, 14, 15, 19, 24, 25, 27, 32, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lemieux et al (US Patent 6,359,054, issued 3/19/02, filed 1/8/99), in view of Emanuele (US Patent 5,674,911, issued 10/7/97).

Lemieux taught methods of delivering to an animal a composition comprising emulsions of non-ionic block copolymers and nucleic acids. See e.g. claim 18. The copolymers are organized as octablocks (see e.g. claim 13 at column 49). The nucleic acid can be an expression vector, antisense, ribozyme, or oligonucleotide (see column 21, lines 15-29). The octablock copolymers useful in the invention include a variety of conventional and reverse orientation octablock copolymers set forth at column 15, lines 8-45 and 25-31, including Pluronics T1101, T1301, T1501 and T110R1, T130R1, and T150R1 (see column 14, lines 34-36 and 54-62). Pluronic T1501 corresponds to the octablock copolymer recited in instant claims 1, 6, 7, 19, 24, and 25. Pluronic T150R1 corresponds to the copolymer in instant claims 27, 32, and 37. Lemieux also taught that the compositions may comprises TWEEN as a surfactant. See column 20, lines 43-47.

Lemieux did not teach a composition comprising both 0.1-5% by weight of a surfactant and 0.5-5% by volume of a low molecular weight alcohol.

Emanuele taught that surfactants such as polyoxyethylenesorbitan (20) monooleate (TWEEN 80), and low molecular weight alcohols such as ethanol may be added to emulsions of non-ionic block copolymer compositions comprising nucleic acids. See column 11, lines 39-58. Further, the ethanol may be in the concentration range of 0.5-5% by volume, and the surfactant may be in a range of approximately 0.1-5% by weight. See e.g. claims 3, 5, and 6.

It would have been obvious to one of ordinary skill in the art at the time of the invention to add the surfactants and low molecular weight alcohols of Emanuele to the compositions of Lemieux. One would have been motivated to do so in order to stabilize the emulsions.

Claims 17, 33, 39, 40, and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Lemieux et al (US Patent 6,359,054, issued 3/19/02, filed 1/8/99).

Lemieux taught methods of delivering to an animal a composition comprising octablock block copolymers and nucleic acids, (see e.g. claim 13 at column 49). The nucleic acid can be an expression vector, antisense, ribozyme, or oligonucleotide (see column 21, lines 15-29). The octablock copolymers useful in the invention include a variety of conventional and reverse orientation octablock copolymers set forth at column 15, lines 8-29, including Pluronics T1101, T1301, T1501 and T110R1, T130R1, and T150R1, each of which has an average hydrophobe percentage of 90%.

Lemieux did not specifically exemplify an octablock copolymer with a hydrophobe percentage of greater than 90% and less than 95%. However, at column 15, line 60 to column 16, line 29, Lemieux taught that the hydrophilic/hydrophobic character of the block copolymer can be optimized depending on the properties of the agent to be delivered. Further, at column 13, lines 1-29, Lemieux taught that the number of POE and POP monomers in each branch of the octablock may range from about 2 to about 800. Thus the molecular weight of the hydrophobic portion is a result effective variable that may be optimized over a range the encompasses that claimed by Applicant. As a result the invention as a whole was prima facie obvious.

Note that claim 33 was omitted from the previous statement of this rejection due to a typographical error. Claim 33 is an independent claim which is anticipated by Lemieux (see above). Claim 40 depends from claim 33, and is obvious over Lemieux

for the reasons set forth above. Because claim 33 is anticipated by Lemieux, and because it embraces all of the limitations of claim 40, it is also obvious in view of Lemieux.

Claims 1-5, 8-13, 16-18, 20-22, 28-30, and 34-36 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Kabanov et al (US Patent 5,656,611, issued 8/12/97).

Kabanov taught compositions comprising polynucleotides and octablock copolymers having molecular weights and relative amounts of POP and POE overlapping those of the instant claims. See abstract and column 7, line 23 to column 8, line 11, especially column 7, lines 40-50). The polynucleotides may be antisense, oligonucleotides, ribozymes, or expression vectors (see column 10, lines 9-28. The copolymers may be of standard or reversed orientation (see column 7, line 64 to column 8, line 3). The compositions of the copolymers, with respect to the amounts and proportions of POE and POP, embrace a wide variety of compounds (see e.g. column 7, lines 48-51 which disclose that POP and POE monomers may be present in each of the four octablock copolymers in amounts of from about 5 to about 400 monomers).

Kabanov did not teach the precise limitations of the claims with respect to the molecular weight of the POP portion of the copolymer, or the relative amounts of POP and POE in the copolymers. However, it would have been obvious to one of ordinary skill in the art at the time of the invention to arrive at the compositions set forth in the claims in the process of optimizing the invention of Kabanov for the disclosed purpose of delivering nucleic acids to cells. Because Kabanov taught a range of compositions which overlaps or embraces

those of the instant invention, Kabanov teaches the general conditions of the claims. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Thus the invention as a whole was *prima facie* obvious.

(10) Response to Argument

Prosecution History

Appellant claimed priority under 35 USC 120 to a variety of US patent applications including prior application 08/138,271 ('271), filed 10/15/1993, and 07/673,289 (filed 3/19/1991). This priority claim was not granted because the instant claims are not supported by the priority documents. All instant claims embrace compositions comprising a nucleic acid and a molecule comprising four copolymers of polyoxyethylene (POE) and polyoxypropylene (POP) attached to an ethylene diamine molecule as set forth in e.g. instant claims 1 or 9. For simplicity these copolymer compounds are hereinafter referred to as octablock copolymers. None of the priority documents provides support for the combination of nucleic acids and octablock copolymers. So, priority was denied and the filing date of the instant claims was considered to be the filing date of the instant application, 7/31/01.

Throughout prosecution, Appellant's arguments regarding the priority date have been based on the '271 and '289 applications. The '289 application discloses octablock copolymers as adjuvants in the delivery of therapeutic agents. The '271 application teaches that nucleic acid sequences as instantly claimed are therapeutic agents, but

does not disclose octablock copolymers. Appellant argued in the response filed 4/15/2004 that the '289 application provided support broadly for the combination of therapeutic agents and octablock copolymers, and because the '271 application extends the definition of therapeutic agents to include nucleic acids as instantly claimed, these documents provide support for the instantly claimed invention. This argument was found unpersuasive in the Office Action of 6/2/04 because neither priority document alone provided support for the combination of octablock copolymers and nucleic acids. Appellant has not pursued this line of argument further. Appellant's arguments have subsequently focused on the issue of whether or not the '271 application fully supports the instant claims, and more specifically, whether or not the '271 application supports octablock copolymers.

Response to Arguments in Appellant's Brief

Appellant's response to the rejections above is found at pages 14-16 of the brief. The essence of Appellant's argument is that the instant application is entitled to a filing date of October 15, 1993 at the latest, and so the Lemieux, Emanuele, and Kabanov references are not valid references under 35 USC 102 or 103.

Appellant argues at page 14 of the brief that the '271 application disclosed nucleic acid sequences in combination with either linear copolymers or octablock copolymers. Appellant argues that the '271 application incorporated by reference US Patent 2,674,619 ('619) and the non-patent reference Schmolka (J. Am. Oil Chemist Soc. 54:110-116 (1977)), and that these references provide support for octablock copolymers. A review of these references shows that they each taught how to make a

broad genus of copolymers of polyoxyethylene (POE) and polyoxypropylene (POP), including several species of linear copolymers and one species of octablock copolymer.

Initially, it should be noted that the non-patent Schmolka article cannot properly be incorporated by reference to provide support for the instantly claimed octablock copolymers. This is because the structure of the octablock copolymers as recited in the instant claims is essential subject material, and essential subject material cannot be incorporated by reference to non-patent publications. See 37 CFR 1.57(c) and MPEP 608.01(p) which state that essential subject material may be incorporated by reference only to a US patent or a US patent application publication. As a result, Appellants arguments at page 15, last full paragraph to page 16, last full paragraph, regarding proper incorporation by reference are unpersuasive as they might apply to the Schmolka reference.

In any case, it is the position of the Office that neither the Schmolka reference nor the '619 patent, as referenced in the priority documents, can properly provide support for the instantly claimed invention because none of the priority documents that disclose the combination of POE/POP copolymers and nucleic acids ever mentions the term "octablock", or refers in any way to octablock-type copolymers. MPEP 608.01 (p) indicates that when incorporating material by reference "[p]articular attention should be directed to specific portions of the referenced document where the subject matter being incorporated may be found." In this case, there is no reference to any particular portion of the '619 patent, or the Schmolka reference, that discloses octablock copolymers, so there is no reason to believe that the Appellant intended in the '271 application to rely upon '619 or Schmolka for disclosure of the species of octablock copolymers.

A review of the '271 specification reveals that the invention disclosed therein was directed to admixtures of a therapeutic compound (e.g. a nucleic acid) and an effective amount of a block copolymer of the general formula:

$$HO(C_2H_4O)_bC_3H_6O)_a(C_2H_4O)_bH,$$

which is the general formula of a poloxamer (a type of linear copolymer), not a branched octablock copolymer (see, e.g. abstract, page 6, lines 5-21, pages 13 and 14, Fig. 1, Table II, and claims 1 and 9). The '271 application never mentions the term "octablock" and does not explicitly disclose any octablock copolymer. The '271 specification indicates at page 17, lines 1-6 that the range of copolymers encompassed by the invention is shown in Fig.1. The '619 and Schmolka references are referred to at page 17, lines 12-18, as providing a description of how to prepare the copolymers presented in Fig. 1. Fig. 1 discloses 21 copolymers, 17 of which are products of BASF corporation having trade names beginning with a prefix 'L', 'P', or 'F'. BASF corporation uses the prefix 'T' to denote octablock copolymers, so none of these 17 copolymers appears to be an octablock copolymer. The remaining 4 copolymers are CRL 336, CRL 1190, CRL 1235, and CRL 8950. There is nothing in the specification to suggest that any of these compounds is an octablock copolymer, and Applicant has provided no evidence or argument indicating such. The '619 patent is also referred to at page 15, lines 20-23 as providing guidance as to how to make "these products". The phrase "these products" is taken to mean the copolymers disclosed at e.g. pages 13 and 14 of the '271 specification, i.e. linear poloxamers. In view of the available evidence, the specification of '271 is directed to poloxamers of the general formula:

$$HO(C_2H_4O)_bC_3H_6O)_a(C_2H_4O)_bH,$$

as recited throughout the '271 specification and claims. The specification is not directed to octablock copolymers, because these copolymers are never mentioned or explicitly disclosed. There are no passages in the '271 specification that direct one of skill in the art to any specific portions of the referenced documents where the claimed octablock copolymers may be found (as required by MPEP 608.01(p), cited above). As a result, there is no reason to believe that the '271 application intended to rely upon '619 or Schmolka for disclosure of the species of octablock copolymers. On the contrary, the '271 application clearly indicates that the invention is directed to poloxamers of the general formula:

$$HO(C_2H_4O)_bC_3H_6O)_a(C_2H_4O)_bH.$$

It follows that even though the '619 patent was properly incorporated by reference, it does not provide support for the instantly claimed embodiments because neither it nor any of the priority documents, including the '271 and '289 applications, discloses or contemplates the combination of octablock copolymers and nucleic acids.

The Examiner agrees that the '619 reference taught how to make a genus of POE- and POP-containing copolymers, including several linear species and one octablock species. See e.g. column 3, line 30 to column 5, line 75, and Examples 2-5, especially column 10, lines 43-47 and column 11, lines 11-19. However, the instant claims are drawn to two general types of octablock copolymers. In one type, one POP polymer is attached to each of the four N atoms of an ethylene diamine molecule, and then POE polymers are attached to the free termini of the POP polymers, resulting in structures similar to those in instant claims 1-8, 17-26, 39, 41, and 42. This is taught in

the '619 reference at column 10, lines 43-69. In the other type of instantly claimed copolymer the arrangement of POP and POE polymers is reversed. POE polymers are attached to each of the four N atoms of an ethylene diamine molecule, and then POP polymers are attached to the free termini of the POE polymers, resulting in the structures in instant claims 9-16, 27-38, and 40. Neither the Schmolka reference nor the '619 reference teaches or contemplates this second type of copolymer. So even if the references could properly support the octablock copolymers in claims 1-8, 17-26, 39, 41, and 42, neither reference can provide support for the octablock copolymers in claims 9-16, 27-38, and 40.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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